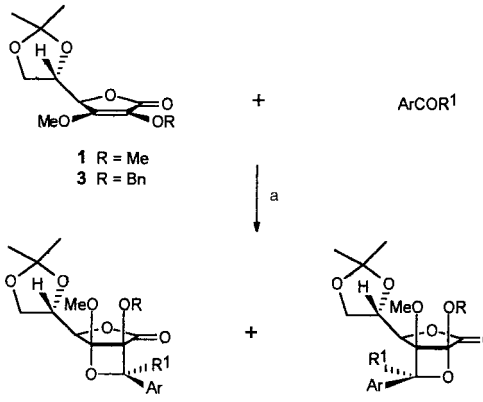
The Paternò–Büchi Reaction of L-Ascorbic Acid**

Shankar R. Thopate, Mukund G. Kulkarni,* and Vedavati G. Puranik

The biological and pharmacological activity as well as the therapeutic potential of L-ascorbic acid and its derivatives have been studied extensively.[1] However, despite the fact that L-ascorbic acid possesses several interesting functionalities, the organic chemistry and synthetic potential of this molecule and its derivatives have never been explored to any significant extent. The complex chemical properties[1] of L-ascorbic acid may have hindered developments in this regard. Alkylation of L-ascorbic acid has been extensively studied, and conditions for both O- and C-alkylations have been worked out.[2] With these alkylation reactions, natural products such as as delesserine, dilaspirolactone aglycon, leucodrin, leudrin, methyl rhodomelol, reflexin, and rhodomelol have been synthesized.[3] Apart from alkylation, however, virtually no other reactions of L-ascorbic acid have been documented, except for reports on the Claisen rearrangement of its O-allyl derivatives.[1]

The conjugated electron-rich enediol unit in L-ascorbic acid is a rather unique and interesting functionality. Such an olefin should be amenable to various noteworthy transformations and might display intriguing reactivity. Enediol or 2-aminoenol moieties in the form of 1,3-dioxol-2-one,[4] 2,3-dihydrooxazol-2-one,[5] and 1,3-dioxole[6] have already yielded corresponding oxetanes through Paternò–Büchi reactions. Enantiomerically pure oxetanes have been synthesized from chiral substrates[7] and with the aid of chiral auxiliaries.[8] Bach and co-workers investigated the stereochemical aspects of oxetane formation, including facial diastereoselection.[9] L-Ascorbic acid constitutes a convenient reactive chiral olefin that should also furnish chiral oxetanes through Paternò–Büchi reactions. Further transformations of the resulting oxetanes by way of ring-opening reactions would afford novel C-2-branched 3-ketosugars and C-3-branched 2-ketosugars. We describe here the preliminary results of our investigations in this area.

Irradiation of a solution of **1** and benzaldehyde in benzene with UV light through a pyrex filter produced compounds **2a** and **2b** in 60 and 25% yield, respectively (Scheme 1). Spectroscopic data and elemental analyses indicate that these



2a R = Me, Ar = Ph, R^1 = H (60%) **2b** R = Me, Ar = Ph, R^1 = H (25%)
4a R = Bn, Ar = Ph, R^1 = H (57%) **4b** R = Bn, Ar = Ph, R^1 = H (28%)
5a R = Bn, Ar = 4-ClC$_6$H$_4$, R^1 = H (40%) **5b** R = Bn, Ar = 4-ClC$_6$H$_4$, R^1 = H (20%)
6a R = Bn, Ar = 4-MeO$_2$C$_6$H$_4$, R^1 = H (42%) **6b** R = Bn, Ar = 4-MeO$_2$C$_6$H$_4$, R^1 = H (23%)
7a R = Bn, Ar = R^1 = Ph (33%) **7b** R = Bn, Ar = R^1 = Ph (65%)

Scheme 1. Paternò–Büchi reactions of **1** and **3**. a) *hν*, C_6H_6, N_2, 30–60 h. Bn = benzyl.

compounds are oxetanes.[10] As compared to **1**, ^{1}H NMR signals for protons in the methoxy groups at C-2 and C-3 in **2a** and **2b** were shifted to the upfield region. These shifts[11] are characteristic, but proved inadequate to permit regio- and stereochemical assignments for these particular oxetanes. However, the observed pattern of chemical shifts might be useful for structural assignments in other oxetanes derived from L-ascorbic acid. Photochemical cycloaddition of benzaldehyde to L-ascorbic acid derivative **3** afforded oxetanes **4a** and **4b** in 57 and 28% yield, respectively (Scheme 1).

The preferred mode of attack for the photoexcited carbonyl group of benzaldehyde on enediols **1** and **3** would presumably be from the less hindered α face, with the aldehyde proton oriented in *endo* fashion. Therefore, one would expect a *cis* orientation of the phenyl residue and alkoxy groups on the oxetane ring for products **2a**, **2b**, **4a**, and **4b**; this orientation was verified unambiguously by X-ray crystallographic analysis of **2a**[12] (Figure 1). This structure determination also made

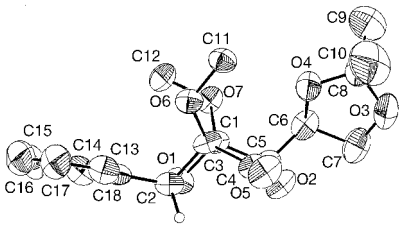


Figure 1. An ORTEP representation of **2a** with the crystallographic numbering of the atoms (thermal ellipsoids are drawn at the 50% probability level).

clear that the major regioisomers formed in the reaction of **1** and **3** with benzaldehyde are **2a** and **4a**, respectively. To investigate the regiochemistry further, substituted benzaldehydes were allowed to react with **3** (Scheme 1). In the case of 4-chlorobenzaldehyde, oxetanes **5a** and **5b** were obtained in 40 and 20% yield, respectively. Similarly, reaction of methyl

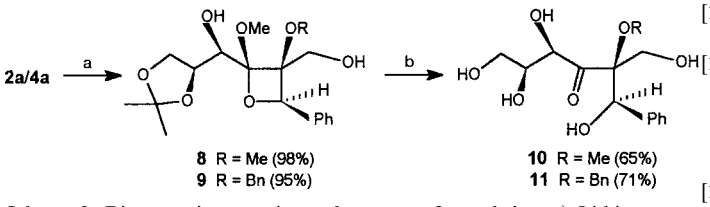
[*] Dr. M. G. Kulkarni, S. R. Thopate
Department of Chemistry
University of Pune
Ganeshkhind, Pune 411007 (India)
Fax: (+91) 212-35-1728
E-mail: mgkul@chem.unipune.ernet.in
Dr. V. G. Puranik
Physical Chemistry Division
National Chemical Laboratory
Pashan, Pune 411008 (India)

[**] Chemistry of L-Ascorbic Acid, Part 2. This work was supported by the Department of Science and Technology, New Delhi. S.R.T. thanks CSIR, New Delhi for awarding an SRF. We wish to thank Dr. H. R. Sonavane and Dr. S. V. Pansare (National Chemical Laboratory, Pune) and Prof. T. Bach (Marburg, Germany) for helpful discussions and suggestions. Part 1: reference [2].

  1433-7851/98/3708-1110 $ 17.50+.50/0

4-formylbenzoate with **3** led to oxetanes **6a** (42%) and **6b** (23%). The regiochemical preferences observed in these reactions are similar to those in the reaction of **3** with benzaldehyde. Photochemical cycloaddition of **3** to benzophenone furnished the two regioisomeric oxetanes **7a** and **7b** in 33 and 65% yield, respectively (Scheme 1). The observed difference in regiochemical preferences in the reactions of **3** with benzaldehydes versus benzophenone indicates that two different mechanisms may be operative. The measured oxidation potential of **3** and the reduction potentials of the benzaldehydes used suggest a photoinduced electron transfer mechanism[13] for reaction of **3** with the benzaldehydes, while reaction with benzophenone most probably occurs by a 1,4-diradical pathway.[14] These mechanisms would indeed account for the regiochemistry observed in the reactions of **1** and **3** with benzaldehydes and benzophenone, but further investigations in this context will be necessary.

The resulting oxetanes are in themselves interesting compounds, and they are also useful synthetic intermediates. Oxetanes are known to yield ring-opened products under various reaction conditions.[15] Analogous transformations of the oxetanes described above could lead to a variety of optically pure materials. Thus, treatment of oxetanes **2a** and **4a** with lithium aluminum hydride gave compounds **8** and **9** in 98 and 95% yield, respectively (Scheme 2). Spectroscopic



Scheme 2. Ring-opening reactions of oxetanes **2a** and **4a**. a) Lithium aluminum hydride, THF, 0°C, 1 h; b) H_2SO_4 (10%), THF, 20°C, 2–6 h. Bn = benzyl.

data for **8** and **9** showed that the lactone group had been reduced. Under aqueous, acidic conditions, oxetanes **8** and **9** were opened to 2-hydroxymethyl-3-ketohexose derivatives **10** (65%) and **11** (71%, Scheme 2). However, attempted selective removal of the benzyl group in oxetane **4a** under hydrogenolytic conditions (H_2, Pd/C, room temperature, atmospheric pressure) did not succeed, and starting material was recovered quantitatively from the reaction mixture.

The results presented here demonstrate that 2-hydroxymethyl-1-phenyl-3-ketohexose derivatives are readily accessible through the Paternò–Büchi adducts derived from L-ascorbic acid. Similarly, a 2-ketohexose derivative might possibly be obtained from **4b.** Further investigations are in progress into the chemistry of the oxetanes and the mechanisms by which they are formed.

Experimental Section

A mixture of **1** or **3** (10 mmol) and freshly distilled benzaldehyde (12 mmol) in dry benzene (125 mL) was purged with dry nitrogen for 5 min. The solution was then irradiated for 30–60 h with UV light (125 W, medium-pressure mercury lamp) in an immersion-well photoreactor at ambient temperature under nitrogen. After completion of the reaction, the solution was washed with aqueous $NaHCO_3$ (10%), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate).

Received: April 23, 1997
Revised version: October 29, 1997 [Z10377IE]
German version: *Angew. Chem.* **1998**, *110*, 1144–1147

Keywords: ascorbic acid · carbohydrates · cycloadditions · heterocycles · Paternò–Büchi reactions

[1] K. Wimalasena, M. P. D. Mahindaratne, *J. Org. Chem.* **1994**, *59*, 3427–3432, and references therein.
[2] M. G. Kulkarni, S. R. Thopate, *Tetrahedron* **1996**, *52*, 1293–1302.
[3] A. J. Poss, R. K. Belter, *J. Org. Chem.* **1988**, *53*, 1535–1540.
[4] a) Y. Araki, J. Nagasawa, Y. Ishido, *J. Chem. Soc. Perkin Trans. 1* **1981**, 12–23; b) *Carbohydr. Res.* **1977**, *58*, C4–C6.
[5] K. H. Scholz, H. G. Heine, W. Hartmann, *Tetrahedron Lett.* **1978**, 1467–1470.
[6] a) J. Mattay, K. Buchkremer, *Heterocycles* **1988**, *27*, 2153–2165; b) *Helv. Chem. Acta* **1988**, *71*, 981–987.
[7] a) K. Matsuura, Y. Araki, Y. Ishido, *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3496–3498; b) K. Matsuura, Y. Araki, Y. Ishido, A. Murai, K. Kushida, *Carbohydr. Res.* **1973**, *29*, 459–468.
[8] a) H. Koch, J. Runsink, H. D. Scharf, *Tetrahedron Lett.* **1983**, *24*, 3217–3220; b) A. Nehrings, H. D. Scharf, J. Runsink, *Angew. Chem.* **1985**, *97*, 882–883; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 877–878.
[9] T. Bach, K. Jödicke, K. Kather, J. Hecht, *Angew. Chem.* **1995**, *107*, 2455–2457; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2271–2273, and references therein.
[10] All new compounds gave satisfactory spectroscopic data and elemental analyses.
[11] In the case of **2a** and **4a** the resonces for the 2-alkoxy and 3-methoxy protos were shifted to higher field by 0.50 to 0.37 ppm relative to those of **1** and **3**. With oxetanes **2b** and **4b** the upfield shift was 1.15 to 1.32 ppm for the 3-methoxy protons and 0.05 to 0.182 ppm for the 2-alkoxy protons.
[12] X-ray structure analysis of (1*S*,4*R*,4′*S*,5*R*,7*R*)-4-(2,2-dimethyl-1,3-dioxolan-4-yl)-1,5-dimethoxy-7-phenyl-3,6-dioxabicyclo[3.2.0]heptan-2-one (**2a**): $C_{18}H_{22}O_7$, $M_r = 350.36$, crystal dimensions $0.13 \times 0.3 \times 0.6$ mm, PC-controlled Enraf–Nonius CAD4 diffractometer, $Mo_{K\alpha}$ radiation ($\lambda = 0.7093$ Å), $\omega/2\theta$ scan mode, scan speed $1^\circ\,min^{-1}$, $a = 6.581(2)$, $b = 26.171(8)$, $c = 10.269(2)$ Å, $V = 1768.6(8)$ Å, $\rho_{calcd} = 1.316\,g\,cm^{-3}$, $\mu\ Mo_{K\alpha} = 0.101\ mm^{-1}$, $Z = 4$, orthorhombic, space group $P2_12_12_1$ (no. 19); of 2931 measured reflections ($h = 0$ to 7, $k = 0$ to 29, $l = 0$ to 11), 2621 were unique and 1974 observed [$F \geq 2\sigma(F)$]; 226 refined parameters, $R = 0.0618$, $WR = 0.171$, refinement on F^2. The structure was solved by direct methods and refined with SHELXL-93. Hydrogen atoms were fixed geometrically on the basis of difference Fourier maps and held fixed during refinement. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as "supplementary publication no. CCDC-100425." Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).
[13] Photoinduced electron transfer is a well-known phenomenon that has been extensively studied[16] and reviewed.[17] It has been demonstrated that the probability of photoinduced electron transfer is a function of the reduction potential of the acceptor and the oxidation potential of the donor through the Rehm–Weller equation.[18] The measured reduction potential of L-ascorbic acid derivatives **1** and **3** was found to be 0.15 V. Cyclic voltammograms of these compounds revealed only the reduction peak, but such data are still applicable for calculation of ΔG values[19a] according to Arnold and Humphreys.[19b] The measured reduction potentials of the aldehydes studied were: benzaldehyde 1.93 V (reported[20] 1.93 V), 4-chlorobenzaldehyde 1.41 V (reported[21] 1.26 V), methyl 4-formylbenzoate 1.23 V. Based on the Rehm–Weller equation, photoinduced electron transfer for L-ascorbic acid derivatives **1** and **3** and the above benzaldehydes has a sufficiently negative

  1433-7851/98/3708-1111 $ 17.50+.50/0

ΔG value (ca. -25 kcal mol^{-1} to ca. -35 kcal mol^{-1}), so a photoinduced electron-transfer mechanism is apparently favored for these photochemical cycloaddition reactions.

[14] a) G. Büchi, C. G. Inman, E. S. Lipinski, *J. Am. Chem. Soc.* **1954**, *76*, 4327 – 4331; b) D. R. Arnold, *Adv. Photochemistry* **1968**, *6*, 301 – 423; c) G. Jones II in *Organic Photochemistry, Vol. 5* (Ed.: A. Padwa), Dekker, New York, **1981**, pp. 1 – 123; d) H. A. J. Carless in *Synthetic Organic Photochemistry* (Ed.: W. M. Horsepool), Plenum, New York, **1984**, pp. 425 – 487; e) S. C. Freilich, K. S. Peters, *J. Am. Chem. Soc.* **1985**, *107*, 3819 – 3822.

[15] a) E. P. Kohler, N. K. Richtmyer, *J. Am. Chem. Soc.* **1930**, *52,* 2038 – 2046; b) D. Scharf, F. Korte, *Tetrahedron Lett.* **1963**, 821 – 823; c) S. H. Schroeter, C. M. Orlando, Jr., *J. Org. Chem.* **1969**, *34*, 1181 – 1187; d) S. H. Schroeter, *ibid.* **1969**, *34*, 1188 – 1191; e) G. Adames, C. Bibby, R. Grigg, *J. Chem. Soc. Chem. Commun.* **1972**, 491 – 492, and references therein; f) G. Jones II, S. B. Schwartz, M. T. Marton, *ibid.* **1973**, 374 – 375, and references therein; g) G. Jones II, M. A. Acquadro, M. A. Carmody, *ibid.* **1975**, 206 – 207; h) J. Mattay, J. Gersdorf, U. Freudenberg, *Tetrahedron Lett.* **1984**, *25*, 817 – 820; i) H. D. Scharf, M. Weuthen, J. Runsink, R. Vassen, *Chem. Ber.* **1988**, *121*, 971 – 976; j) T. Bach, *Tetrahedron Lett.* **1994**, *35*, 5855 – 5858; k) *Liebigs Ann.* **1995**, 1045 – 1053; l) T. Bach, K. Kather, *J. Org. Chem.* **1996**, *61*, 3900 – 3901; m) T. Bach, C. Lange, *Tetrahedron Lett.* **1996**, *37*, 4363 – 4364.

[16] a) J. Mattay, *Synthesis* **1989**, 233 – 252; b) J. Mattay, M. Vondenhof, *Top. Curr. Chem.* **1991**, *159*, 219 – 255; c) A. Albini, D. R. Arnold, *Can. J. Chem.* **1978**, *56*, 2985 – 2993; d) J. Mattay, A. Heidbreder, *Tetrahedron Lett.* **1992**, *33*, 1973 – 1976; e) A. G. Griesbeck, O. Sadlek, K. Polborn, *Liebigs Ann.* **1996**, 545 – 549; f) J. Mattay, J. Gersdorf, H. Leismann, S. Steenken, *Angew. Chem.* **1984**, *96*, 240 – 241; *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 249 – 250; g) J. Mattay, J. Gersdorf, K. Buchkremer, *Chem. Ber.* **1987**, *120*, 307 – 318.

[17] a) J. Mattay, *Angew. Chem.* **1987**, *99*, 849 – 870; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 825 – 845; b) J. Mattay, F. Müller, *Chem. Rev.* **1993**, *93*, 99 – 117.

[18] D. Rehm, A. Weller, *Isr. J. Chem.* **1970**, *8*, 259 – 271.

[19] a) J. Mattay, J. Gersdorf, H. Görner, *J. Am. Chem. Soc.* **1987**, *109*, 1203 – 1209; b) D. R. Arnold, R. W. R. Humphreys, *ibid.* **1979**, *101*, 2743 – 2744.

[20] S. G. Mairanovskii, I. E. Valashek, G. I. Samokhvalov, *Elektrokhimiya* **1967**, *3*, 611.

[21] J. W. Sease, F. G. Burton, S. L. Nickol, *J. Am. Chem. Soc.* **1968**, *90*, 2595 – 2598.

A Porphyrin as a Binucleating Ligand: Preparation and Crystal Structure of a Porphyrin Complex Containing a Coordinated B_2O_2 Ring

Warwick J. Belcher, Matthis Breede, Penelope J. Brothers,* and Clifton E. F. Rickard

The enormously wide utility of the porphyrin ligand in coordination chemistry derives in part from the fact that there is a distance of 2 Å from the center of the square-planar N_4 coordination site to one nitrogen atom; a broad range of elements in various oxidation states can be accommodated. Even larger elements can be coordinated as out-of-plane complexes, and to some extent smaller elements can be accommodated by ruffling of the ligand and compression of the porphyrin core. We recently demonstrated that boron can form a porphyrin complex[1] which contains two boron atoms as an F-B-O-B-F moiety threaded through the cavity in the porphyrin, such that each boron atom is coordinated to two different porphyrin nitrogen donor atoms. One boron atom lies approximately in the plane of the ligand, while the other is displaced significantly out of this plane (overall C_s symmetry). This compound, $[B_2OF_2(ttp)]$ (**1**, ttp = dianion of 5,10,15,20-tetra-*p*-tolylporphyrin), was prepared by the reaction of $BF_3 \cdot OEt_2$ with the free base porphyrin $H_2(ttp)$ in the presence of a trace of water. The structure of **1** was confirmed by an X-ray crystal structure determination of $[B_2OF_2(T\textit{p}Clpp)]$ (**2**, T*p*Clpp = dianion of 5,10,15,20-tetra-*p*-chlorophenylporphyrin).[1]

The corresponding reaction of $BCl_3 \cdot MeCN$ with $H_2(ttp)$ in chlorobenzene containing a trace of water[2] is more complex than that of $BF_3 \cdot OEt_2$. Initially a blue-green precipitate forms which is highly reactive and releases the bound boron atoms to provide the free base porphyrin if dissolved in a neutral or acidic solvent. When the precipitate is dissolved in dichloromethane and subjected to chromatography on basic alumina, $[B_2O(OH)_2(ttp)]$ (**3**) is formed. This compound is analogous to the fluoroboron complex $[B_2OF_2(ttp)]$ but contains hydroxo groups in place of the fluorine substituents.[1]

The blue-green precipitate formed in the reaction of $BCl_3 \cdot MeCN$ with $H_2(ttp)$ persists in solution for a few minutes, which is long enough to obtain its ^{1}H NMR spectrum in $CDCl_3$. The spectrum shows the compound to have higher symmetry than $[B_2OX_2(ttp)]$ (X = F, OH), and the tolyl methyl groups appear as two singlets in a 1:1 ratio. By careful control of the reaction conditions and use of $H_2(T\textit{p}Clpp)$ as the porphyrin and benzene as the solvent, it proved possible to isolate crystals of the blue-green compound following recrystallization from $CHCl_3$ saturated with $BCl_3 \cdot MeCN$. X-ray crystallography revealed a second structural type for a boron porphyrin and a new coordination mode for the porphyrin ligand.[3]

The compound $[B_2O_2(BCl_3)_2(T\textit{p}Clpp)]$ (**4**) contains a four-membered B_2O_2 ring coordinated in the cavity of the porphyrin; the plane of the B_2O_2 ring is perpendicular to the ligand plane (Figure 1). Two porphyrin nitrogen atoms coordinate to each boron atom, and the two boron atoms are essentially coplanar with the porphyrin. Each bridging oxygen atom is coordinated to a BCl_3 molecule. The crystals contain two independent half-molecules that are related through a center of symmetry. Each B_2O_2 ring has two unique B–O distances which are almost the same (av 1.49(2) Å), and the B1 $\cdots$ B1′ distance across the ring is close to 2.1 Å. The B2–O1 distances involving the coordinated BCl_3 molecules average 1.49(2) Å.

To accommodate two boron atoms in the same plane as the porphyrin, the macrocycle has undergone an elongation along one axis to result in a rectangular rather than a square core. The N1 $\cdots$ N2 distance parallel to the B $\cdots$ B axis averages 3.63 Å, over 1.1 Å longer than the N1 $\cdots$ N2′ distance within the N-B-N chelate rings (2.49 Å). This elongation is reflected in the bond angles at C4, C5, and C6, which have opened

[*] Dr. P. J. Brothers, Dr. W. J. Belcher, M. Breede, Prof. C. E. F. Rickard
Department of Chemistry
University of Auckland
Private Bag 92019, Auckland (New Zealand)
Fax: (+64) 9-373-7422
E-mail: p.brothers@auckland.ac.nz

  1433-7851/98/3708-1112 $ 17.50+.50/0